MTF

Edison Corporate Center
125 May Street, Suite 300
Edison, NJ 08837
(732) 661-0202

December 23, 1999

0302 '99 DEC 28 A9:43

Food and Drug Administration
Dockets Management Branch, HCFA-305
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Docket No. 97N-484S

Dear Sir or Madam:

On behalf of the Musculoskeletal Transplant Foundation (MTF), I am responding to the Proposed Approach to Regulation of Cellular and Tissue Based Products. MTF appreciates this opportunity to respond to the Food and Drug Administration (FDA) proposed rule 21 CFR Part 1271 "Suitability Determination for Donors of Human Cellular and Tissue-Based Products". Because MTF's scope of activity falls predominantly within the FDA's term of "conventional tissue," my remarks will be addressed to those areas that affect my organization.

Founded in 1987, MTF is the nation's largest non-profit musculoskeletal tissue recovery organization and has recovered more than 18,000 tissue donors to date. The Foundation's membership consists of leading medical/academic/research institutions, as well as 26 tissue/organ recovery organizations throughout the country. The majority of these recovery organizations represent nearly 1/3 of the nation's OPOs.

The Foundation is also an accredited member of the American Association of Tissue Banks (AATB) and has actively participated with the AATB to develop standards for tissue banking. We have formulated our comments to the discussion document based upon these experiences.

MTF supports the FDA's principle of donor screening and testing to prevent the transmission of communicable diseases. However, MTF is concerned the definitions of "homologous use" and "minimal manipulation" under the proposed Part 1271, as currently written, are vague and open to broad interpretation. MTF considers these definitions to be the cornerstone of the proposed rule.

We hope that our comments and suggestions will be taken into serious consideration.

Sincerely,

Joel C. Osborne, Director of Quality
Assurance and Regulatory Affairs

Attachment

97N-484S

C 221

MUSCULOSKELETAL TRANSPLANT FOUNDATION COMMENTS TO PROPOSED RULE 21 CFR PART 1271 "SUITABILITY DETERMINATION FOR DONORS OF HUMAN CELLULAR AND TISSUE-BASED PRODUCTS"

1. General Comment: Retrospective Application of 21 CFR 1271

MTF is adamantly opposed to the retrospective application of any regulation or guidance documents to tissue recovered prior to its issuance. In many cases, conventional tissues, such as frozen or freeze-dried tissues, have a shelf life of up to five years. The retrospective application of this regulation could potentially cause the needless loss of safe human tissue in order to comply with the new regulation. FDA has already set a past precedent by not requiring retrospective application of the final rule (21 CFR 1270) to tissues recovered prior to its issuance.

MTF recommends that FDA add the following wording to the proposed rule, which is contained in the preamble to current final rule 21 CFR 1270 section III C.

"The final rule (21 CFR 1271) will have an effective date of 180 days after the date of publication and will apply to human tissues and cells after the effective date. For tissues and cells procured prior to the effective date of the final rule (21 CFR 1271), the previous rule 21 CFR 1270 applies."

2. The use of the term "product"

MTF recommends removing the word "product" to identify human tissues and cells throughout the document. In general, human tissues and cells are gifts donated by the next-of-kin. From a strict legal interpretation, establishments that distribute human tissues and cells perform a "service" and do not sell a "product." It is illegal in the United States to buy or sell human tissue or cells. The use of the term "product" reinforces the erroneous concept that human tissues and cells are commodities that are bought and sold. If the FDA defines tissues and cells as "products" this could potentially set a legal precedent to apply strict product liability laws to future legal cases involving human tissues or cells. Finally, the term "product" dehumanizes the precious gift that a family gives and may actually discourage donor families from donating tissues or cells.

3. Preamble Section III B.1. Proposed Section 1271.3(b) Definition of "Establishment" Proposed Section 1271.3(f) Definition of "Manufacturer"

MTF recommends the definition specifies laboratories that only perform infectious disease testing services or hospitals or physicians that only store tissues shall not be required to register. Requiring registration for these laboratories, not involved with other manufacturing steps, should not be required because the current and proposed rule states that all testing must be performed in laboratories certified under the Clinical Laboratory Improvement Amendment of 1988 (CLIA).

Hospitals and physician's offices that only store human tissues or cells prior to transplantation should not be required to register, provided that the hospital or physician does not engage in other activities included in the definition of "manufacturer." There are literally thousands of hospitals and physicians offices that store human tissues and cells prior to transplantation. Requiring hospitals and physician offices to register would cause an unnecessary burden for those facilities and the FDA.

We suggest revising the following proposed definition:

(b)... The term (establishment) also includes any individual partnership, corporation, association, or other legal entity engaged in the manufacturer of human cellular or tissue-based products. An individual or other legal entity under contract to a registered establishment engaged solely in the following activities are not required to register: Facilities that recover tissues or cells; laboratories that perform donor infectious disease testing; hospitals and physician's offices that store tissues or cells intended for transplantation.

4. Preamble Section III B.1. Proposed Section 1271.3(d & g) Definition of "Homologous Use" and "Minimal Manipulation"

As discussed in our previous comments on the "Proposed Approach" document, the terms "minimally manipulated" and "homologous use" need to be more clearly defined. It is our opinion that the current definitions are vague and would be subject to broad interpretation by FDA. MTF is concerned that these definitions, if applied to some conventional tissues that have been used successfully by clinicians for many years, could lead to reclassification of these tissues as medical devices or biologics.

For example, a bone dowel that has been shaped in the form of a screw and is used to hold two pieces of bone together could be considered minimally processed (because it is shaped) and is for homologous use (to hold two pieces of bone together). However, a screw made out of bone might be determined a device by FDA because it would have many of the same characteristics of a screw made from metal and is intended for the same application.

MTF recommends that there be an open dialogue between representatives from the industry in cooperation with the FDA Tissue Reference Group to resolve issues related to the classification of tissue and cell forms.

5. Proposed Section 1271.3(y) Biohazard Labeling of Untested Tissues

Labeling recovered tissue "untested for Biohazard" may present an issue regarding transporting tissues or cells from a recovery location to a tissue or cell storage facility. In some cases, recovered tissues or cells may be transported by a commercial air carrier. Commercial carriers are reluctant to transport a container labeled "Biohazard."

Without any clarification to the wording used in proposed regulation, a compliance or regulatory authority could interpret that the outer label of the transport container must state "untested for Biohazard." MTF agrees that the tissue container of any unprocessed tissue in quarantine be labeled "untested for Biohazard." We recommend that the Proposed regulation clarify that the tissue container, not necessarily the tissue transport container, be labeled with "untested for Biohazard."

6. Preamble Section III B.1. Proposed Section 1271.3(o) Definition of "Donor Medical History Interview"

The proposed definition of "donor medical history interview" implies that interviews with sources of information about the prospective donor must be in person. Interviews should not be limited to an in-person, face-to-face interview. MTF recommends that the proposed definition should be revised specifically to include written exchanges, telephonic communication, and other forms of communication.

7. Proposed Section 1271.3(y) Procedure for identifying additional relevant "communicable disease agents or diseases"

FDA should specify in the final rule itself the procedures it will use to identify additional "relevant communicable disease agents and diseases." The industry might be able to provide the FDA with recommendations regarding the need for adding new diseases or disease agents and help in planning the implementation of new infectious disease tests when they become available.

8. Proposed Section 1271.80(b), Requirement that the donor specimen be collected at the time of recovery or within 48 hours after recovery

MTF agrees with FDA's concern that a time limit on sample recovery should be established. However, MTF is concerned that this proposed requirement is not feasible and will result in the needless loss of donor tissues and cells. The proposed requirement also runs counter to FDA's current recommendation in previous guidance documents to test pretransfusion specimens whenever possible. In many cases, blood samples, especially pretransfused samples, are recovered pre-mortem. Because of problems with false positive test results, it is far better to test pre-mortem samples rather than post-mortem samples. It would therefore be reasonable and feasible to state that a donor specimen must be collected within 48 hours of death. This would allow for pre-mortem and pretransfused samples as well as post-transfusion samples to be collected.

Therefore, MTF recommends that FDA consider revising the proposed rule as follows:

1271.80(b) ... the donor specimen shall be collected within 48 hours of death.

9. FDA Tissue Reference Group

MTF agrees in principle with the multi-center approach for regulating products that combine tissue or cellular based products with drugs, devices and biologics. However, even with the full cooperation of all of the branches of the FDA working together through the Tissue Reference Group (TRG), the process of evaluating, classifying and approving these combination tissues appears to be a bit confusing, and could possibly be a potentially time consuming process.

MTF recommends that the regulation stipulate a reasonable time limit for FDA to review and approve combination products. In addition, the proposed regulation should clearly indicate that combination products may indeed follow a process of approval equivalent to a 510K if appropriate.

With respect to the TRG proceedings, FDA should institute the following general procedures for any action taken or proposed which would have broad effects on the industry.

- TRG meetings should be announced by publication in the Federal Register or in some formal fashion, with a general description of the issues to be discussed.
- TRG meetings should be open to the public, except for portions of the meeting involving proprietary information.
- The proceedings of the TRG's including jurisdictional determination should be published.

Align top of FedEx PowerShip Label here.

JOEL OSBORNE
MUSCULOSKELETAL TRNSPLNT FOUND
125 MAY ST STE 300
EDISON NJ 08837
(732)661-0202

SHIP DATE: 23DEC99
ACCOUNT # 143451763
MAN-WGT:1 LBS

TO:
FOOD & DRUG ADMINISTRATION
DOCKETS MANAGEMENT BRANCH, HCFA-305
5630 FISHER LANE, ROOM 1061
ROCKVILLE MD 20852

( ) -

271 9397 563

FedEx. POWERSHIP 3

271 9397 563

REF:

2DAY

MON
AA

CAD # 665322 23DEC99

Trk# 271 9397 563

FedEx Letter

IAD

20852-MD-US

SA EDG

PART # 147923 FORMAT # 077 RIT 02/98

World On Time®
Letter